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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  May 12   EXTEND option available in structure searching
 NEWS  4  May 12   Polymer links for the POLYLINK command completed in REGISTRY
 NEWS  5  May 27   New UPM (Update Code Maximum) field for more efficient patent
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 NEWS  7  Jun 22   STN Patent Forums to be held July 19-22, 2004
 NEWS  8  Jun 28   Additional enzyme-catalyzed reactions added to CASREACT
 NEWS  9  Jun 28   ANTE, AQUALINE, BIOENG, CIVILENG, ENVIROENG, MECHENG,
                   and WATER from CSA now available on STN(R)
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                   resulting in a closer connection to BABS

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               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 26 APRIL 2004
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FILE 'EMBASE' ENTERED AT 12:17:03 ON 22 JUL 2004
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=> s (RAR antagonist)
L1          289 (RAR ANTAGONIST)

=> s l1 and (BMP? or (osteogenic protein) or OPS or cytokine#)
L2           29 L1 AND (BMP? OR (OSTEOGENIC PROTEIN) OR OPS OR CYTOKINE#)

=> s l2 and (chondrogen?)
L3            8 L2 AND (CHONDROGEN?)

=> s l3 and (solution or suspension or gel or matirx or cream or gel or film or
paste or capsule or pill or tablet or encapsul? or Microcapsule# or micropart?)
   4 FILES SEARCHED...
L4            3 L3 AND (SOLUTION OR SUSPENSION OR GEL OR MATIRX OR CREAM OR
                GEL OR FILM OR PASTE OR CAPSULE OR PILL OR TABLET OR ENCAPSUL?
                OR MICROCAPSULE# OR MICROPART?)

=> s l4 and liposom?
L5            3 L4 AND LIPOSOM?

=> d l5 1-3 ibib abs

L5   ANSWER 1 OF 3  USPATFULL on STN
ACCESSION NUMBER:         2003:181419  USPATFULL
TITLE:                    Compositions and methods for affecting osteogenesis
INVENTOR(S):              Underhill, T. Michael, Ontario, CANADA
                          Sampaio, Arthur V., Ontario, CANADA
                          Weston, Andrea D., Ontario, CANADA

                               NUMBER        KIND    DATE
                          ---------------- ------ --------
PATENT INFORMATION:       US 2003125252      A1   20030703
APPLICATION INFO.:        US 2002-221602     A1   20020912  (10)
                          WO 2001-CA317           20010313
DOCUMENT TYPE:            Utility
FILE SEGMENT:             APPLICATION
LEGAL REPRESENTATIVE:     MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH,
                          NC, 27627
NUMBER OF CLAIMS:         72
EXEMPLARY CLAIM:          1
NUMBER OF DRAWINGS:       6 Drawing Page(s)
LINE COUNT:               1833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB    The invention relates to compositions for promoting and inhibiting
      osteogenesis and to methods for treating bone abnormalities resulting
      from injury, toxicity or disease and for ex vivo bone tissue
      engineering.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
```

L5 ANSWER 2 OF 3 USPATFULL on STN

ACCESSION NUMBER: 2003:47877 USPATFULL

TITLE: Use of ligands for treatment of diseases responsive to retinoids

INVENTOR(S): Chambon, Pierre, Blaesheim, FRANCE
Borrelli, Emiliana, Strasbourg, FRANCE
Ghyselinck, Norbert B., Strasbourg, FRANCE
Dupe, Valerie, London, UNITED KINGDOM
Mark, Manuel, Morchwiller, FRANCE
Metzger, Daniel, Strasbourg, FRANCE

PATENT ASSIGNEE(S): Institut National de la Santa et de la Recherche Medicale, Paris, FRANCE (non-U.S. corporation)
Centre National de la Recherche Scientifique, Paris, FRANCE (non-U.S. corporation)
Universite Louis Pasteur, Strasbourg, FRANCE (non-U.S. corporation)
Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 6521814 | B1 | 20030218 |
| APPLICATION INFO.: | US 1998-218446 | | 19981222 (9) |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1997-68471P | 19971222 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Reynolds, Deborah J.
ASSISTANT EXAMINER: Sorbello, Eleanor
LEGAL REPRESENTATIVE: Sterne, Kessler Goldstein & Fox
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 124 Drawing Figure(s); 51 Drawing Page(s)
LINE COUNT: 5178
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods for treatment of neurological disease by administering an agent which interacts with a retinoid receptor associated with the neurological disease. The invention is also related to a method of modulating dopamine receptor synthesis by introducing an agent that interacts with a retinoid receptor associated with the dopamine receptor synthesis. The invention is further related to a transgenic animal, e.g., mouse, and mammalian cell line, which is deficient in the normal synthesis of one or more receptors of RAR$\alpha$, $\beta$, $\gamma$ and RXR, and cell line thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L5 ANSWER 3 OF 3 EUROPATFULL COPYRIGHT 2004 WILA on STN

GRANTED PATENT - ERTEILTES PATENT - BREVET DELIVRE

ACCESSION NUMBER: 1131067 EUROPATFULL EW 200420 FS PS

TITLE: COMPOSITION AND USE OF RAR ANTAGONISTS FOR PROMOTING **CHONDROGENESIS.**
ZUBEREITUNG UND VERWENDUNG VON RAR ANTAGONISTEN ZUR FORDERUNG DER **CHONDROGENESE.**
COMPOSITION A BASE D'ANTAGONISTES DES RAR ET SON UTILISATION POUR FAVORISER LA **CHONDROGENESE.**

INVENTOR(S): UNDERHILL, Tully Michael, Univ. Western of Ontario, Div. of Oral Biology, School of Dentistry, London, Ontario N6A 5C1, CA;
WESTON, Andrea, Dawn, Univ.of Western Ontario, The

| | |
|---|---|
| | Faculty of Med. & Dentistry, Dep.of Phys., London, Ontario N6A 5C1, CA |
| PATENT ASSIGNEE(S): | The University of Western Ontario, Office of Industry Liason, Stevenson-Lawson Building, Room 319, London, Ontario N6A 5B8, CA |
| PATENT ASSIGNEE NO: | 1820961 |
| AGENT: | Holliday, Louise Caroline, D Young & Co, 21 New Fetter Lane, London EC4A 1DA, GB |
| AGENT NUMBER: | 95451 |
| OTHER SOURCE: | MEPB2004021 EP 1131067 B1 0035 |
| SOURCE: | Wila-EPS-2004-H20-T1 |
| DOCUMENT TYPE: | Patent |
| LANGUAGE: | Anmeldung in Englisch; Veroeffentlichung in Englisch |
| DESIGNATED STATES: | R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE; R AL; R LT; R LV; R MK; R RO; R SI |
| PATENT INFO.PUB.TYPE: | EPB1 EUROPAEISCHE PATENTSCHRIFT (Internationale Anmeldung) |

PATENT INFORMATION:

| PATENT NO. | KIND | DATE |
|---|---|---|
| EP 1131067 | B1 | 20040512 |
| 'OFFENLEGUNGS' DATE: | | 20010912 |
| APPLICATION INFO.: EP 1999-955613 | | 19991119 |
| PRIORITY APPLN. INFO.: CA 1998-2254429 | | 19981119 |
| RELATED DOC. INFO.: WO 99-CA1106 | | 991119 INTAKZ |
| WO 2000030635 | | 000602 INTPNR |
| REFERENCE PAT. INFO.: WO 98-08546 A | | WO 99-24415 A |
| US 5827500 A | | |

REF. NON-PATENT-LIT.: KOYAMA E ET AL: "Retinoid signaling is required for chondrocyte maturation and endochondral bone formation during limb skeletogenesis." DEVELOPMENTAL BIOLOGY, (1999 APR 15) 208 (2) 375-91., XP000879298 PATENT ABSTRACTS OF JAPAN vol. 1998, no. 10, 31 August 1998 (1998-08-31) & JP10114757 A (SHUDO KOICHI), 6 May 1998 (1998-05-06) STANDEVEN A M ET AL: "Retinoid-induced epiphyseal plate closure in guinea pigs." FUNDAMENTAL AND APPLIED TOXICOLOGY, (1996 NOV) 34 (1) 91-8., XP000879170 KOYAMA, E. ET AL: "Retinoids and their nuclear receptors promote the completion of chondrocyte maturation during limb skeletogenesis." MOLECULAR BIOLOGY OF THE CELL, (NOV., 1997) VOL. 8, NO. SUPPL., PP. 71A. MEETING INFO.: 37TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY WASHINGTON, D.C., USA DECEMBER 13-17, 1997 AMERICAN SOCIETY FOR CELL BIOLOGY., XP000879148 NUKA S (REPRINT) ET AL: "All-trans retinoic acid inhibits dexamethasone-induced ALP activity and mineralization in human osteoblastic cell line SV HFO" CELL STRUCTURE AND FUNCTION, (FEB 1997) VOL. 22, NO. 1, PP. 27-32. PUBLISHER: JAPAN SOC CELL BIOLOGY, SHIMOTACHIURI OGAWA-HIGASHI, KAMIKYOKU KYOTO 602, JAPAN. ISSN: 0386-7196., XP000879088 SAPPORO MED UNIV, SCH MED, DEPT PATHOL, CHUO KU, S1, W17, SAPPORO, HOKKAIDO 060, JAPAN (Reprint);SAPPORO MED UNIV, SCH MED, DEPT ORTHOPAED SURG, CHUO KU, SAPPORO, HOKKAIDO 060, JAPAN VON SCHROEDER H P ET AL: "The effects of natural and synthetic retinoids on the differentiation of RCJ C5.18 chondrogenic cells." TERATOLOGY, (1994 JUL) 50 (1) 54-62., XP000653320 JIANG: "Modulation of limb bud chondrogenesis by retinoic acid and retinoic acid receptors." DEVELOPMENTAL BIOLOGY, vol. 39, no. 4, 1995, XP000884176

=> d l3 1-8 ibib abs

L3 ANSWER 1 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:368088 CAPLUS
DOCUMENT NUMBER: 133:828
TITLE: Composition and use of RAR antagonists for promoting **chondrogenesis**
INVENTOR(S): Underhill, Tully Michael; Weston, Andrea Dawn
PATENT ASSIGNEE(S): The University of Western Ontario, Can.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000030635 | A1 | 20000602 | WO 1999-CA1106 | 19991119 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1131067 | A1 | 20010912 | EP 1999-955613 | 19991119 |
| EP 1131067 | B1 | 20040512 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002530331 | T2 | 20020917 | JP 2000-583518 | 19991119 |
| AU 764394 | B2 | 20030814 | AU 2000-12552 | 19991119 |
| AU 2000012552 | A5 | 20000613 | | |
| US 2002061514 | A1 | 20020523 | US 2001-957456 | 20010921 |

PRIORITY APPLN. INFO.:
CA 1998-2254429 A 19981119
WO 1999-CA1106 W 19991119
US 2000-234242P P 20000921

AB The invention provides compns. comprising a **RAR antagonist** for promoting **chondrogenesis**, as well as methods employing such compns. for treating cartilage and associated bone abnormalities resulting from injury or disease and for ex vivo tissue engineering.
REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 8 CAPLUS COPYRIGHT 2004 ACS on STN
ACCESSION NUMBER: 2000:147914 CAPLUS
DOCUMENT NUMBER: 132:261066
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways
AUTHOR(S): Weston, Andrea D.; Rosen, Vicki; Chandraratna, Roshantha A. S.; Underhill, T. Michael
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine & Dentistry, The University of Western Ontario, London, ON, N6A 5C1, Can.
SOURCE: Journal of Cell Biology (2000), 148(4), 679-690
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during

limb out-growth. Several signaling mols. have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARα in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects. Further anal. of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:181419 USPATFULL
TITLE: Compositions and methods for affecting osteogenesis
INVENTOR(S): Underhill, T. Michael, Ontario, CANADA
Sampaio, Arthur V., Ontario, CANADA
Weston, Andrea D., Ontario, CANADA

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 2003125252 | A1 | 20030703 | |
| APPLICATION INFO.: | US 2002-221602 | A1 | 20020912 | (10) |
| | WO 2001-CA317 | | 20010313 | |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 72
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to compositions for promoting and inhibiting osteogenesis and to methods for treating bone abnormalities resulting from injury, toxicity or disease and for ex vivo bone tissue engineering.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 8 USPATFULL on STN
ACCESSION NUMBER: 2003:47877 USPATFULL
TITLE: Use of ligands for treatment of diseases responsive to retinoids
INVENTOR(S): Chambon, Pierre, Blaesheim, FRANCE
Borrelli, Emiliana, Strasbourg, FRANCE
Ghyselinck, Norbert B., Strasbourg, FRANCE
Dupe, Valerie, London, UNITED KINGDOM
Mark, Manuel, Morchwiller, FRANCE
Metzger, Daniel, Strasbourg, FRANCE

PATENT ASSIGNEE(S): Institut National de la Santa et de la Recherche Medicale, Paris, FRANCE (non-U.S. corporation)
Centre National de la Recherche Scientifique, Paris, FRANCE (non-U.S. corporation)
Universite Louis Pasteur, Strasbourg, FRANCE (non-U.S. corporation)
Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 6521814 | B1 | 20030218 |
| APPLICATION INFO.: | US 1998-218446 | | 19981222 (9) |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1997-68471P | 19971222 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Reynolds, Deborah J.
ASSISTANT EXAMINER: Sorbello, Eleanor
LEGAL REPRESENTATIVE: Sterne, Kessler Goldstein & Fox
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 124 Drawing Figure(s); 51 Drawing Page(s)
LINE COUNT: 5178
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods for treatment of neurological disease by administering an agent which interacts with a retinoid receptor associated with the neurological disease. The invention is also related to a method of modulating dopamine receptor synthesis by introducing an agent that interacts with a retinoid receptor associated with the dopamine receptor synthesis. The invention is further related to a transgenic animal, e.g., mouse, and mammalian cell line, which is deficient in the normal synthesis of one or more receptors of RARα, β, γ and RXR, and cell line thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 8 EUROPATFULL COPYRIGHT 2004 WILA on STN

GRANTED PATENT - ERTEILTES PATENT - BREVET DELIVRE

ACCESSION NUMBER: 1131067 EUROPATFULL EW 200420 FS PS
TITLE: COMPOSITION AND USE OF RAR ANTAGONISTS FOR PROMOTING **CHONDROGENESIS.**
ZUBEREITUNG UND VERWENDUNG VON RAR ANTAGONISTEN ZUR FORDERUNG DER **CHONDROGENESE.**
COMPOSITION A BASE D'ANTAGONISTES DES RAR ET SON UTILISATION POUR FAVORISER LA **CHONDROGENESE.**
INVENTOR(S): UNDERHILL, Tully Michael, Univ. Western of Ontario, Div. of Oral Biology, School of Dentistry, London, Ontario N6A 5C1, CA;
WESTON, Andrea, Dawn, Univ.of Western Ontario, The Faculty of Med. & Dentistry, Dep.of Phys., London, Ontario N6A 5C1, CA
PATENT ASSIGNEE(S): The University of Western Ontario, Office of Industry Liason, Stevenson-Lawson Building, Room 319, London, Ontario N6A 5B8, CA
PATENT ASSIGNEE NO: 1820961
AGENT: Holliday, Louise Caroline, D Young & Co, 21 New Fetter Lane, London EC4A 1DA, GB
AGENT NUMBER: 95451
OTHER SOURCE: MEPB2004021 EP 1131067 B1 0035

SOURCE: Wila-EPS-2004-H20-T1
DOCUMENT TYPE: Patent
LANGUAGE: Anmeldung in Englisch; Veroeffentlichung in Englisch
DESIGNATED STATES: R AT; R BE; R CH; R CY; R DE; R DK; R ES; R FI; R FR; R GB; R GR; R IE; R IT; R LI; R LU; R MC; R NL; R PT; R SE; R AL; R LT; R LV; R MK; R RO; R SI
PATENT INFO.PUB.TYPE: EPB1 EUROPAEISCHE PATENTSCHRIFT (Internationale Anmeldung)
PATENT INFORMATION:

| PATENT NO | KIND | DATE |
|---|---|---|
| EP 1131067 | B1 | 20040512 |

'OFFENLEGUNGS' DATE: 20010912
APPLICATION INFO.: EP 1999-955613 19991119
PRIORITY APPLN. INFO.: CA 1998-2254429 19981119
RELATED DOC. INFO.: WO 99-CA1106 991119 INTAKZ
WO 2000030635 000602 INTPNR
REFERENCE PAT. INFO.: WO 98-08546 A WO 99-24415 A
US 5827500 A
REF. NON-PATENT-LIT.: KOYAMA E ET AL: "Retinoid signaling is required for chondrocyte maturation and endochondral bone formation during limb skeletogenesis." DEVELOPMENTAL BIOLOGY, (1999 APR 15) 208 (2) 375-91., XP000879298 PATENT ABSTRACTS OF JAPAN vol. 1998, no. 10, 31 August 1998 (1998-08-31) & JP10114757 A (SHUDO KOICHI), 6 May 1998 (1998-05-06) STANDEVEN A M ET AL: "Retinoid-induced epiphyseal plate closure in guinea pigs." FUNDAMENTAL AND APPLIED TOXICOLOGY, (1996 NOV) 34 (1) 91-8., XP000879170 KOYAMA, E. ET AL: "Retinoids and their nuclear receptors promote the completion of chondrocyte maturation during limb skeletogenesis." MOLECULAR BIOLOGY OF THE CELL, (NOV., 1997) VOL. 8, NO. SUPPL., PP. 71A. MEETING INFO.: 37TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY WASHINGTON, D.C., USA DECEMBER 13-17, 1997 AMERICAN SOCIETY FOR CELL BIOLOGY., XP000879148 NUKA S (REPRINT) ET AL: "All-trans retinoic acid inhibits dexamethasone-induced ALP activity and mineralization in human osteoblastic cell line SV HFO" CELL STRUCTURE AND FUNCTION, (FEB 1997) VOL. 22, NO. 1, PP. 27-32. PUBLISHER: JAPAN SOC CELL BIOLOGY, SHIMOTACHIURI OGAWA-HIGASHI, KAMIKYOKU KYOTO 602, JAPAN. ISSN: 0386-7196., XP000879088 SAPPORO MED UNIV, SCH MED, DEPT PATHOL, CHUO KU, S1, W17, SAPPORO, HOKKAIDO 060, JAPAN (Reprint);SAPPORO MED UNIV, SCH MED, DEPT ORTHOPAED SURG, CHUO KU, SAPPORO, HOKKAIDO 060, JAPAN VON SCHROEDER H P ET AL: "The effects of natural and synthetic retinoids on the differentiation of RCJ C5.18 chondrogenic cells." TERATOLOGY, (1994 JUL) 50 (1) 54-62., XP000653320 JIANG: "Modulation of limb bud chondrogenesis by retinoic acid and retinoic acid receptors." DEVELOPMENTAL BIOLOGY, vol. 39, no. 4, 1995, XP000884176

L3 ANSWER 6 OF 8 MEDLINE on STN
ACCESSION NUMBER: 2000153508 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10684250
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways.
AUTHOR: Weston A D; Rosen V; Chandraratna R A; Underhill T M
CORPORATE SOURCE: Division of Oral Biology, School of Dentistry, The University of Western Ontario, London, Ontario, Canada.
SOURCE: Journal of cell biology, (2000 Feb 21) 148 (4) 679-90. Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000313

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARalpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L3 ANSWER 7 OF 8 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN
ACCESSION NUMBER: 2000:142678 BIOSIS
DOCUMENT NUMBER: PREV200000142678
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways.
AUTHOR(S): Weston, Andrea D.; Rosen, Vicki; Chandraratna, Roshantha A. S.; Underhill, T. Michael [Reprint author]
CORPORATE SOURCE: School of Dentistry, Faculty of Medicine and Dentistry, University of Western Ontario, London, ON, N6A 5C1, Canada
SOURCE: Journal of Cell Biology, (Feb. 21, 2000) Vol. 148, No. 4, pp. 679-690. print.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Apr 2000
Last Updated on STN: 4 Jan 2002

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARalpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast

differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L3 ANSWER 8 OF 8 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000316638 EMBASE

TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways.

AUTHOR: Weston A.D.; Rosen V.; Chandraratna R.A.S.; Underhill T.M.

CORPORATE SOURCE: T.M. Underhill, School of Dentistry, Faculty of Medicine/Dentistry, University of Western Ontario, London, Ont. N6A 5C1, Canada. tunderhi@julian.uwo.ca

SOURCE: Journal of Cell Biology, (21 Feb 2000) 148/4 (679-690). Refs: 63
ISSN: 0021-9525 CODEN: JCLBA3

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 021 Developmental Biology and Teratology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARα in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

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 NEWS  10 MAR 22  KOREAPAT now updated monthly; patent information enhanced
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 NEWS  13 MAR 22  REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS  14 APR 04  EPFULL enhanced with additional patent information and new
                  fields
 NEWS  15 APR 04  EMBASE - Database reloaded and enhanced
 NEWS  16 APR 18  New CAS Information Use Policies available online
 NEWS  17 APR 25  Patent searching, including current-awareness alerts (SDIs),
                  based on application date in CA/CAplus and USPATFULL/USPAT2
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                  applications.
 NEWS  18 APR 28  Improved searching of U.S. Patent Classifications for
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               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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=> s (RAR antagonist#)
L1 510 (RAR ANTAGONIST#)

=> s l1 and ((bone morphogenic protein?) or BMP? or (osteogenic protein?) or OP? or cytokine?)
3 FILES SEARCHED...
5 FILES SEARCHED...
L2 136 L1 AND ((BONE MORPHOGENIC PROTEIN?) OR BMP? OR (OSTEOGENIC PROTE IN?) OR OP? OR CYTOKINE?)

=> s l2 and chondrogen?
L3 12 L2 AND CHONDROGEN?

=> d l3 1-12 ibib abs

L3 ANSWER 1 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:368088 CAPLUS
DOCUMENT NUMBER: 133:828
TITLE: Composition and use of **RAR antagonists** for promoting **chondrogenesis**
INVENTOR(S): Underhill, Tully Michael; Weston, Andrea Dawn
PATENT ASSIGNEE(S): The University of Western Ontario, Can.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000030635 | A1 | 20000602 | WO 1999-CA1106 | 19991119 |

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

| | | | | |
|---|---|---|---|---|
| CA 2349555 | AA | 20000602 | CA 1999-2349555 | 19991119 |
| EP 1131067 | A1 | 20010912 | EP 1999-955613 | 19991119 |
| EP 1131067 | B1 | 20040512 | | |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO

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|---|---|---|---|---|
| JP 2002530331 | T2 | 20020917 | JP 2000-583518 | 19991119 |
| AU 764394 | B2 | 20030814 | AU 2000-12552 | 19991119 |
| AU 2000012552 | A5 | 20000613 | | |
| AT 266396 | E | 20040515 | AT 1999-955613 | 19991119 |
| ES 2219076 | T3 | 20041116 | ES 1999-955613 | 19991119 |
| CA 2357549 | AA | 20020321 | CA 2001-2357549 | 20010921 |
| US 2002061514 | A1 | 20020523 | US 2001-957456 | 20010921 |
| HK 1041633 | A1 | 20041008 | HK 2002-101649 | 20020304 |
| PRIORITY APPLN. INFO.: | | | CA 1998-2254429 A | 19981119 |
| | | | WO 1999-CA1106 W | 19991119 |
| | | | US 2000-234242P P | 20000921 |

AB The invention provides compns. comprising a **RAR antagonist** for promoting **chondrogenesis**, as well as methods employing such compns. for treating cartilage and associated bone abnormalities resulting from injury or disease and for ex vivo tissue engineering.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 12 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:147914 CAPLUS
DOCUMENT NUMBER: 132:261066

TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways

AUTHOR(S): Weston, Andrea D.; Rosen, Vicki; Chandraratna, Roshantha A. S.; Underhill, T. Michael
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine & Dentistry, The University of Western Ontario, London, ON, N6A 5C1, Can.

SOURCE: Journal of Cell Biology (2000), 148(4), 679-690
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb out-growth. Several signaling mols. have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARα in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects. Further anal. of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to **operate** independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce

cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 3 OF 12 USPATFULL on STN

| | | | |
|---|---|---|---|
| ACCESSION NUMBER: | 2005:63066 USPATFULL | | |
| TITLE: | Expansion of renewable stem cell populations using modulators of PI 3-kinase | | |
| INVENTOR(S): | Peled, Tony, Mevaseret Zion, ISRAEL<br>Grynspan, Frida, Mevasseret Zion, ISRAEL | | |
| | NUMBER | KIND | DATE |
| PATENT INFORMATION: | US 2005054103 | A1 | 20050310 |
| APPLICATION INFO.: | US 2004-795215 | A1 | 20040304 (10) |
| RELATED APPLN. INFO.: | Continuation-in-part of Ser. No. WO 2003-IL235, filed on 18 Mar 2003, PENDING Continuation-in-part of Ser. No. WO 2003-IL681, filed on 17 Aug 2003, PENDING | | |
| | NUMBER | DATE | |
| PRIORITY INFORMATION: | US 2003-452545P | 20030307 (60) | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | MINTZ, LEVIN, COHN, FERRIS, GLOVSKY, AND POPEO, P.C., ONE FINANCIAL CENTER, BOSTON, MA, 02111 | | |
| NUMBER OF CLAIMS: | 147 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 41 Drawing Page(s) | | |
| LINE COUNT: | 6805 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Provided are ex vivo and in vivo methods of expanding renewable stem cells using modulators of PI 3-kinase activity, expanded populations of renewable stem cells, and uses thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 12 USPATFULL on STN

| | | | |
|---|---|---|---|
| ACCESSION NUMBER: | 2005:11733 USPATFULL | | |
| TITLE: | Retinoid receptor pan-antagonists for stimulating **chondrogenesis** | | |
| INVENTOR(S): | Underhill, Michael Tully, Ontario, CANADA<br>Weston, Andrea D, Ontario, CANADA | | |
| | NUMBER | KIND | DATE |
| PATENT INFORMATION: | US 2005009868 | A1 | 20050113 |
| APPLICATION INFO.: | US 2004-489750 | A1 | 20040827 (10) |
| | WO 2002-CA1421 | | 20020917 |
| | NUMBER | DATE | |
| PRIORITY INFORMATION: | US 2001-322874P | 20010917 (60) | |
| DOCUMENT TYPE: | Utility | | |
| FILE SEGMENT: | APPLICATION | | |
| LEGAL REPRESENTATIVE: | MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627 | | |
| NUMBER OF CLAIMS: | 20 | | |
| EXEMPLARY CLAIM: | 1 | | |
| NUMBER OF DRAWINGS: | 10 Drawing Page(s) | | |
| LINE COUNT: | 1777 | | |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods and compositions for inducing or enhancing **chondrogenesis** in vivo and/or ex vivo. More specifically, the invention is directed to the use of RAR pan-antagonist compositions for the treatment, repair and engineering of cartilage.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 5 OF 12 USPATFULL on STN

| | | | |
|---|---|---|---|
| ACCESSION NUMBER: | 2005:10492 USPATFULL | | |
| TITLE: | Expansion of renewable stem cell populations | | |
| INVENTOR(S): | Peled, Tony, Mevaseret Zion, ISRAEL<br>Treves, Avi, Mevaseret Zion, ISRAEL<br>Rosen, Oren, Jerusalem, ISRAEL | | |

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2005008624 | A1 | 20050113 |
| APPLICATION INFO.: | US 2004-774843 | A1 | 20040209 (10) |
| RELATED APPLN. INFO.: | Continuation of Ser. No. WO 2003-IL64, filed on 26 Jan 2003, PENDING | | |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | IL 2002-152904 | 20021117 |
| | US 2002-404137P | 20020819 (60) |
| | US 2002-376183P | 20020430 (60) |

| | |
|---|---|
| DOCUMENT TYPE: | Utility |
| FILE SEGMENT: | APPLICATION |
| LEGAL REPRESENTATIVE: | MINTZ, LEVIN, COHN, FERRIS, GLOVSKY, AND POPEO, P.C., ONE FINANCIAL CENTER, BOSTON, MA, 02111 |
| NUMBER OF CLAIMS: | 64 |
| EXEMPLARY CLAIM: | CLM-1-400 |
| NUMBER OF DRAWINGS: | 17 Drawing Page(s) |
| LINE COUNT: | 5497 |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Ex vivo and in vivo methods of expansion of renewable stem cells, expanded populations of renewable stem cells and their uses.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 6 OF 12 USPATFULL on STN

| | | | |
|---|---|---|---|
| ACCESSION NUMBER: | 2003:181419 USPATFULL | | |
| TITLE: | Compositions and methods for affecting osteogenesis | | |
| INVENTOR(S): | Underhill, T. Michael, Ontario, CANADA<br>Sampaio, Arthur V., Ontario, CANADA<br>Weston, Andrea D., Ontario, CANADA | | |

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2003125252 | A1 | 20030703 |
| APPLICATION INFO.: | US 2002-221602 | A1 | 20020912 (10) |
| | WO 2001-CA317 | | 20010313 |

| | |
|---|---|
| DOCUMENT TYPE: | Utility |
| FILE SEGMENT: | APPLICATION |
| LEGAL REPRESENTATIVE: | MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627 |
| NUMBER OF CLAIMS: | 72 |
| EXEMPLARY CLAIM: | 1 |
| NUMBER OF DRAWINGS: | 6 Drawing Page(s) |
| LINE COUNT: | 1833 |

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to compositions for promoting and inhibiting osteogenesis and to methods for treating bone abnormalities resulting from injury, toxicity or disease and for ex vivo bone tissue

engineering.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 7 OF 12 USPATFULL on STN
ACCESSION NUMBER: 2003:47877 USPATFULL
TITLE: Use of ligands for treatment of diseases responsive to retinoids
INVENTOR(S): Chambon, Pierre, Blaesheim, FRANCE
Borrelli, Emiliana, Strasbourg, FRANCE
Ghyselinck, Norbert B., Strasbourg, FRANCE
Dupe, Valerie, London, UNITED KINGDOM
Mark, Manuel, Morchwiller, FRANCE
Metzger, Daniel, Strasbourg, FRANCE
PATENT ASSIGNEE(S): Institut National de la Santa et de la Recherche Medicale, Paris, FRANCE (non-U.S. corporation)
Centre National de la Recherche Scientifique, Paris, FRANCE (non-U.S. corporation)
Universite Louis Pasteur, Strasbourg, FRANCE (non-U.S. corporation)
Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 6521814 | B1 | 20030218 | |
| APPLICATION INFO.: | US 1998-218446 | | 19981222 | (9) |

| | NUMBER | DATE | |
|---|---|---|---|
| PRIORITY INFORMATION: | US 1997-68471P | 19971222 | (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Reynolds, Deborah J.
ASSISTANT EXAMINER: Sorbello, Eleanor
LEGAL REPRESENTATIVE: Sterne, Kessler Goldstein & Fox
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 124 Drawing Figure(s); 51 Drawing Page(s)
LINE COUNT: 5178
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to methods for treatment of neurological disease by administering an agent which interacts with a retinoid receptor associated with the neurological disease. The invention is also related to a method of modulating dopamine receptor synthesis by introducing an agent that interacts with a retinoid receptor associated with the dopamine receptor synthesis. The invention is further related to a transgenic animal, e.g., mouse, and mammalian cell line, which is deficient in the normal synthesis of one or more receptors of RAR$\alpha$, $\beta$, $\gamma$ and RXR, and cell line thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 8 OF 12 MEDLINE on STN
ACCESSION NUMBER: 2000153508 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10684250
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways.
AUTHOR: Weston A D; Rosen V; Chandraratna R A; Underhill T M
CORPORATE SOURCE: Division of Oral Biology, School of Dentistry, The University of Western Ontario, London, Ontario, Canada.
SOURCE: Journal of cell biology, (2000 Feb 21) 148 (4) 679-90. Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000313

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARalpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to **operate** independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L3 ANSWER 9 OF 12 EPFULL COPYRIGHT 2005 EPO/FIZ KA on STN

ACCESSION NUMBER: 1999:96730 EPFULL
UPDATE DATE PUBLICAT.: 20050504
DATA UPDATE DATE: 20050504
DATA UPDATE WEEK: 200518
TITLE (ENGLISH): COMPOSITION AND USE OF **RAR ANTAGONISTS** FOR PROMOTING **CHONDROGENESIS**
TITLE (FRENCH): COMPOSITION A BASE D'ANTAGONISTES DES RAR ET SON UTILISATION POUR FAVORISER LA **CHONDROGENESE**
TITLE (GERMAN): ZUBEREITUNG UND VERWENDUNG VON RAR ANTAGONISTEN ZUR FORDERUNG DER **CHONDROGENESE**
INVENTOR(S): UNDERHILL, Tully Michael, Univ. Western of Ontario, Div. of Oral Biology, School of Dentistry, London, Ontario N6A 5C1, CA; WESTON, Andrea, Dawn, Univ.of Western Ontario, The Faculty of Med. & Dentistry, Dep.of Phys., London, Ontario N6A 5C1, CA
PATENT APPLICANT(S): The University of Western Ontario, (University of Western Ontario, The; Western Ontario, The University of; Ontario, The University of Western), Office of Industry Liason, Stevenson-Lawson Building, Room 319, London, Ontario N6A 5B8, CA
PATENT APPL. NUMBER: 1820961
AGENT: Holliday, Louise Caroline, D Young & Co 120 Holborn, London EC1N 2DY, GB
AGENT NUMBER: 95451
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English
LANGUAGE OF PROCEDURE: English

LANGUAGE OF TITLE: German; English; French
DOCUMENT TYPE: Patent
PATENT INFO TYPE: EPB1 Granted patent
PATENT INFORMATION:
PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---|---|---|
| NUMBER | KIND | DATE |
| EP 1131067 | B1 | 20040512 |
| WO 2000030635 | | 20000602 |

DESIGNATED STATES: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE
APPLICATION INFO.: EP 1999-955613 A 19991119
WO 1999-CA1106 A 19991119
PRIORITY INFO.: CA 1998-2254429 A 19981119
CITED NON PATENT LIT.: KOYAMA E ET AL: "Retinoid signaling is required for chondrocyte maturation and endochondral bone formation during limb skeletogenesis." DEVELOPMENTAL BIOLOGY, (1999 APR 15) 208 (2) 375-91. , XP000879298;

PATENT ABSTRACTS OF JAPAN vol. 1998, no. 10, 31 August 1998 (1998-08-31) & JP 10 114757 A (SHUDO KOICHI), 6 May 1998 (1998-05-06);

STANDEVEN A M ET AL: "Retinoid-induced epiphyseal plate closure in guinea pigs." FUNDAMENTAL AND APPLIED TOXICOLOGY, (1996 NOV) 34 (1) 91-8. , XP000879170;

KOYAMA, E. ET AL: "Retinoids and their nuclear receptors promote the completion of chondrocyte maturation during limb skeletogenesis." MOLECULAR BIOLOGY OF THE CELL, (NOV., 1997) VOL. 8, NO. SUPPL., PP. 71A. MEETING INFO.: 37TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY WASHINGTON, D.C., USA DECEMBER 13-17, 1997 AMERICAN SOCIETY FOR CELL BIOLOGY. , XP000879148;

NUKA S (REPRINT) ET AL: "All-trans retinoic acid inhibits dexamethasone-induced ALP activity and mineralization in human osteoblastic cell line SV HFO" CELL STRUCTURE AND FUNCTION, (FEB 1997) VOL. 22, NO. 1, PP. 27-32. PUBLISHER: JAPAN SOC CELL BIOLOGY, SHIMOTACHIURI OGAWA-HIGASHI, KAMIKYOKU KYOTO 602, JAPAN. ISSN: 0386-7196., XP000879088 SAPPORO MED UNIV, SCH MED, DEPT PATHOL, CHUO KU, S1, W17, SAPPORO, HOKKAIDO 060, JAPAN (Reprint);SAPPORO MED UNIV, SCH MED, DEPT ORTHOPAED SURG, CHUO KU, SAPPORO, HOKKAIDO 060, JAPAN;

VON SCHROEDER H P ET AL: "The effects of natural and synthetic retinoids on the differentiation of RCJ C5.18 chondrogenic cells." TERATOLOGY, (1994 JUL) 50 (1) 54-62. , XP000653320;

JIANG: "Modulation of limb bud chondrogenesis by retinoic acid and retinoic acid receptors." DEVELOPMENTAL BIOLOGY, vol. 39, no. 4, 1995, XP000884176

CITED PATENT LIT.:

| | |
|---|---|
| WO 9808546 | A |
| WO 9924415 | A |
| US 5827500 | A |

L3 ANSWER 10 OF 12 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:142678 BIOSIS
DOCUMENT NUMBER: PREV200000142678
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways.
AUTHOR(S): Weston, Andrea D.; Rosen, Vicki; Chandraratna, Roshantha A.

S.; Underhill, T. Michael [Reprint author]
CORPORATE SOURCE: School of Dentistry, Faculty of Medicine and Dentistry, University of Western Ontario, London, ON, N6A 5C1, Canada
SOURCE: Journal of Cell Biology, (Feb. 21, 2000) Vol. 148, No. 4, pp. 679-690. print.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Apr 2000
Last Updated on STN: 4 Jan 2002

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARalpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to **operate** independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L3 ANSWER 11 OF 12 EMBASE 
on STN
ACCESSION NUMBER: 2000316638 EMBASE
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways.
AUTHOR: Weston A.D.; Rosen V.; Chandraratna R.A.S.; Underhill T.M.
CORPORATE SOURCE: T.M. Underhill, School of Dentistry, Faculty of Medicine/Dentistry, University of Western Ontario, London, Ont. N6A 5C1, Canada. tunderhi@julian.uwo.ca
SOURCE: Journal of Cell Biology, (21 Feb 2000) Vol. 148, No. 4, pp. 679-690.
Refs: 63
ISSN: 0021-9525 CODEN: JCLBA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 021 Developmental Biology and Teratology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000921
Last Updated on STN: 20000921

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARα in transgenic animals interferes with **chondrogenesis**

and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to **operate** independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L3 ANSWER 12 OF 12 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:171908 SCISEARCH
THE GENUINE ARTICLE: 287NB
TITLE: Regulation of skeletal progenitor differentiation by the **BMP** and retinoid signaling pathways
AUTHOR: Weston A D; Rosen V; Chandraratna R A S; Underhill T M (Reprint)
CORPORATE SOURCE: UNIV WESTERN ONTARIO, SCH DENT, FAC MED & DENT, DIV ORAL BIOL, LONDON, ON N6A 5C1, CANADA (Reprint); UNIV WESTERN ONTARIO, SCH DENT, FAC MED & DENT, DIV ORAL BIOL, LONDON, ON N6A 5C1, CANADA; UNIV WESTERN ONTARIO, DEPT PHYSIOL, FAC MED & DENT, LONDON, ON N6A 5C1, CANADA; GENET INST INC, CAMBRIDGE, MA 02140; ALLERGAN PHARMACEUT INC, RETINOID RES GRP, IRVINE, CA 92623
COUNTRY OF AUTHOR: CANADA; USA
SOURCE: JOURNAL OF CELL BIOLOGY, (21 FEB 2000) Vol. 148, No. 4, pp. 679-690.
Publisher: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021.
ISSN: 0021-9525.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 63

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RAR alpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E,, C.B, Beck, K. Schughart, E, Linney: and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of **BMPs**, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or **BMP**-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations.

In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that **BMP** and RAR-signaling pathways appear to **operate** independently to coordinate skeletal development, and that retinoid signaling can function in a **BMP**-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

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| NEWS | 15 | APR 25 | Patent searching, including current-awareness alerts (SDIs), based on application date in CA/CAplus and USPATFULL/USPAT2 may be affected by a change in filing date for U.S. applications. |
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                  August
 NEWS  28 AUG 11  STN AnaVist workshops to be held in North America
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               AND CURRENT DISCOVER FILE IS DATED 13 JUNE 2005

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=> s (RAR Antagonist#)
L1 527 (RAR ANTAGONIST#)

=> S l1 and chondrogen?
L2 18 L1 AND CHONDROGEN?

=> d l2 1-18 ibib abs

L2 ANSWER 1 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:242177 CAPLUS
DOCUMENT NUMBER: 138:265692
TITLE: Retinoid receptor pan-antagonists for stimulating **chondrogenesis**
INVENTOR(S): Underhill, Tulley Michael; Weston, Andrea D.
PATENT ASSIGNEE(S): The University of Western Ontario, Can.
SOURCE: PCT Int. Appl., 70 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2003024473 | A2 | 20030327 | WO 2002-CA1421 | 20020917 |
| WO 2003024473 | A3 | 20030807 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2459949 | AA | 20030327 | CA 2002-2459949 | 20020917 |
| EP 1427399 | A2 | 20040616 | EP 2002-760008 | 20020917 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| US 2005009868 | A1 | 20050113 | US 2004-489750 | 20040827 |
| PRIORITY APPLN. INFO.: | | | US 2001-322874P | P 20010917 |
| | | | WO 2002-CA1421 | W 20020917 |

AB The invention provides methods and compns. for inducing or enhancing **chondrogenesis** in vivo and/or ex vivo. More specifically, the invention discloses the use of RAR pan-antagonist compns. for the treatment, repair and engineering of cartilage.

L2 ANSWER 2 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:368088 CAPLUS
DOCUMENT NUMBER: 133:828
TITLE: Composition and use of **RAR antagonists** for promoting **chondrogenesis**

INVENTOR(S): Underhill, Tully Michael; Weston, Andrea Dawn
PATENT ASSIGNEE(S): The University of Western Ontario, Can.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000030635 | A1 | 20000602 | WO 1999-CA1106 | 19991119 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2349555 | AA | 20000602 | CA 1999-2349555 | 19991119 |
| EP 1131067 | A1 | 20010912 | EP 1999-955613 | 19991119 |
| EP 1131067 | B1 | 20040512 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002530331 | T2 | 20020917 | JP 2000-583518 | 19991119 |
| AU 764394 | B2 | 20030814 | AU 2000-12552 | 19991119 |
| AU 2000012552 | A5 | 20000613 | | |
| AT 266396 | E | 20040515 | AT 1999-955613 | 19991119 |
| ES 2219076 | T3 | 20041116 | ES 1999-955613 | 19991119 |
| CA 2357549 | AA | 20020321 | CA 2001-2357549 | 20010921 |
| US 2002061514 | A1 | 20020523 | US 2001-957456 | 20010921 |
| HK 1041633 | A1 | 20041008 | HK 2002-101649 | 20020304 |
| PRIORITY APPLN. INFO.: | | | CA 1998-2254429 A | 19981119 |
| | | | WO 1999-CA1106 W | 19991119 |
| | | | US 2000-234242P P | 20000921 |

AB The invention provides compns. comprising a **RAR antagonist** for promoting **chondrogenesis**, as well as methods employing such compns. for treating cartilage and associated bone abnormalities resulting from injury or disease and for ex vivo tissue engineering.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 3 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:147914 CAPLUS
DOCUMENT NUMBER: 132:261066
TITLE: Regulation of skeletal progenitor differentiation by the BMP and retinoid signaling pathways
AUTHOR(S): Weston, Andrea D.; Rosen, Vicki; Chandraratna, Roshantha A. S.; Underhill, T. Michael
CORPORATE SOURCE: Department of Physiology, Faculty of Medicine & Dentistry, The University of Western Ontario, London, ON, N6A 5C1, Can.
SOURCE: Journal of Cell Biology (2000), 148(4), 679-690
CODEN: JCLBA3; ISSN: 0021-9525
PUBLISHER: Rockefeller University Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb out-growth. Several signaling mols. have been identified that are important in specifying the pattern of these skeletal primordia. Very

little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARα in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects. Further anal. of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of BMPs, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or BMP-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that BMP and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a BMP-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

REFERENCE COUNT: 63 THERE ARE 63 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 4 OF 18 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:4772 CAPLUS

DOCUMENT NUMBER: 132:135439

TITLE: Retinoic acid is a potent regulator of growth plate **chondrogenesis**

AUTHOR(S): De Luca, Francesco; Uyeda, Jennifer A.; Mericq, Veronica; Mancilla, Edna E.; Yanovski, Jack A.; Barnes, Kevin M.; Zile, Maija H.; Baron, Jeffrey

CORPORATE SOURCE: Developmental Endocrinology Branch, Institute of Child Health and Human Development, National Institutes of Health, Bethesda, MD, 20892, USA

SOURCE: Endocrinology (2000), 141(1), 346-353
CODEN: ENDOAO; ISSN: 0013-7227

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Vitamin A deficiency and excess both cause abnormalities in mammalian longitudinal bone growth. Because all-trans retinoic acid (RA) is synthesized from vitamin A, we hypothesized that RA regulates growth plate **chondrogenesis.** Consistent with this hypothesis, a single oral dose of RA reduced the height of the rat proximal tibial growth plate. To determine whether RA acts directly on growth plate, fetal rat metatarsal bones were cultured in the presence of RA. In this system, RA inhibited longitudinal bone growth by three mechanisms: (1) decreased chondrocyte proliferation, (assessed by 3H-thymidine incorporation), particularly in the proliferative zone of the growth plate; (2) decreased matrix synthesis (assessed by 35SO4 incorporation into glycosaminoglycans); and (3) decreased cell hypertrophy (determined histol.). The growth-inhibiting effects of RA were completely reversed by a retinoic acid receptor (**RAR**) **antagonist.** In the absence of exogenous RA, this antagonist accelerated bone growth, as did an RA-specific neutralizing antibody, suggesting that endogenous RA neg. regulates growth plate **chondrogenesis.** We conclude that RA, acting through RARs, neg. regulates longitudinal bone growth by inhibiting growth plate chondrocyte proliferation, chondrocyte hypertrophy, and matrix synthesis.

REFERENCE COUNT: 42 THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L2 ANSWER 5 OF 18 USPATFULL on STN

ACCESSION NUMBER: 2005:63066 USPATFULL

TITLE: Expansion of renewable stem cell populations using

modulators of PI 3-kinase
INVENTOR(S): Peled, Tony, Mevaseret Zion, ISRAEL
Grynspan, Frida, Mevasseret Zion, ISRAEL

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2005054103 | A1 | 20050310 |
| APPLICATION INFO.: | US 2004-795215 | A1 | 20040304 (10) |

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. WO 2003-IL235, filed on 18 Mar 2003, PENDING Continuation-in-part of Ser. No. WO 2003-IL681, filed on 17 Aug 2003, PENDING

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 2003-452545P | 20030307 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MINTZ, LEVIN, COHN, FERRIS, GLOVSKY, AND POPEO, P.C., ONE FINANCIAL CENTER, BOSTON, MA, 02111
NUMBER OF CLAIMS: 147
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 41 Drawing Page(s)
LINE COUNT: 6805
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Provided are ex vivo and in vivo methods of expanding renewable stem cells using modulators of PI 3-kinase activity, expanded populations of renewable stem cells, and uses thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 6 OF 18 USPATFULL on STN
ACCESSION NUMBER: 2005:11733 USPATFULL
TITLE: Retinoid receptor pan-antagonists for stimulating **chondrogenesis**
INVENTOR(S): Underhill, Michael Tully, Ontario, CANADA
Weston, Andrea D, Ontario, CANADA

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2005009868 | A1 | 20050113 |
| APPLICATION INFO.: | US 2004-489750 | A1 | 20040827 (10) |
| | WO 2002-CA1421 | | 20020917 |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 2001-322874P | 20010917 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 1777
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to methods and compositions for inducing or enhancing **chondrogenesis** in vivo and/or ex vivo. More specifically, the invention is directed to the use of RAR pan-antagonist compositions for the treatment, repair and engineering of cartilage.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 7 OF 18 USPATFULL on STN
ACCESSION NUMBER: 2005:10492 USPATFULL

TITLE: Expansion of renewable stem cell populations
INVENTOR(S): Peled, Tony, Mevaseret Zion, ISRAEL
Treves, Avi, Mevaseret Zion, ISRAEL
Rosen, Oren, Jerusalem, ISRAEL

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2005008624 | A1 | 20050113 |
| APPLICATION INFO.: | US 2004-774843 | A1 | 20040209 (10) |

RELATED APPLN. INFO.: Continuation of Ser. No. WO 2003-IL64, filed on 26 Jan 2003, PENDING

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | IL 2002-152904 | 20021117 |
| | US 2002-404137P | 20020819 (60) |
| | US 2002-376183P | 20020430 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MINTZ, LEVIN, COHN, FERRIS, GLOVSKY, AND POPEO, P.C., ONE FINANCIAL CENTER, BOSTON, MA, 02111
NUMBER OF CLAIMS: 64
EXEMPLARY CLAIM: CLM-1-400
NUMBER OF DRAWINGS: 17 Drawing Page(s)
LINE COUNT: 5497
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Ex vivo and in vivo methods of expansion of renewable stem cells, expanded populations of renewable stem cells and their uses.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 8 OF 18 USPATFULL on STN
ACCESSION NUMBER: 2003:181419 USPATFULL
TITLE: Compositions and methods for affecting osteogenesis
INVENTOR(S): Underhill, T. Michael, Ontario, CANADA
Sampaio, Arthur V., Ontario, CANADA
Weston, Andrea D., Ontario, CANADA

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 2003125252 | A1 | 20030703 |
| APPLICATION INFO.: | US 2002-221602 | A1 | 20020912 (10) |
| | WO 2001-CA317 | | 20010313 |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 72
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to compositions for promoting and inhibiting osteogenesis and to methods for treating bone abnormalities resulting from injury, toxicity or disease and for ex vivo bone tissue engineering.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 9 OF 18 USPATFULL on STN
ACCESSION NUMBER: 2003:47877 USPATFULL
TITLE: Use of ligands for treatment of diseases responsive to retinoids
INVENTOR(S): Chambon, Pierre, Blaesheim, FRANCE

Borrelli, Emiliana, Strasbourg, FRANCE
Ghyselinck, Norbert B., Strasbourg, FRANCE
Dupe, Valerie, London, UNITED KINGDOM
Mark, Manuel, Morchwiller, FRANCE
Metzger, Daniel, Strasbourg, FRANCE

PATENT ASSIGNEE(S): Institut National de la Santa et de la Recherche Medicale, Paris, FRANCE (non-U.S. corporation)
Centre National de la Recherche Scientifique, Paris, FRANCE (non-U.S. corporation)
Universite Louis Pasteur, Strasbourg, FRANCE (non-U.S. corporation)
Bristol-Myers Squibb Company, Princeton, NJ, United States (U.S. corporation)

| | NUMBER | KIND | DATE |
|---|---|---|---|
| PATENT INFORMATION: | US 6521814 | B1 | 20030218 |
| APPLICATION INFO.: | US 1998-218446 | | 19981222 (9) |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 1997-68471P | 19971222 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Reynolds, Deborah J.
ASSISTANT EXAMINER: Sorbello, Eleanor
LEGAL REPRESENTATIVE: Sterne, Kessler Goldstein & Fox
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 124 Drawing Figure(s); 51 Drawing Page(s)
LINE COUNT: 5178
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods for treatment of neurological disease by administering an agent which interacts with a retinoid receptor associated with the neurological disease. The invention is also related to a method of modulating dopamine receptor synthesis by introducing an agent that interacts with a retinoid receptor associated with the dopamine receptor synthesis. The invention is further related to a transgenic animal, e.g., mouse, and mammalian cell line, which is deficient in the normal synthesis of one or more receptors of RAR$\alpha$, $\beta$, $\gamma$ and RXR, and cell line thereof.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L2 ANSWER 10 OF 18 EPFULL COPYRIGHT 2005 EPO/FIZ KA on STN

ACCESSION NUMBER: 1999:96730 EPFULL
UPDATE DATE PUBLICAT.: 20050504
DATA UPDATE DATE: 20050504
DATA UPDATE WEEK: 200518
TITLE (ENGLISH): COMPOSITION AND USE OF **RAR ANTAGONISTS** FOR PROMOTING **CHONDROGENESIS**
TITLE (FRENCH): COMPOSITION A BASE D'ANTAGONISTES DES RAR ET SON UTILISATION POUR FAVORISER LA **CHONDROGENESE**
TITLE (GERMAN): ZUBEREITUNG UND VERWENDUNG VON RAR ANTAGONISTEN ZUR FORDERUNG DER **CHONDROGENESE**
INVENTOR(S): UNDERHILL, Tully Michael, Univ. Western of Ontario, Div. of Oral Biology, School of Dentistry, London, Ontario N6A 5C1, CA; WESTON, Andrea, Dawn, Univ.of Western Ontario, The Faculty of Med. & Dentistry, Dep.of Phys., London, Ontario N6A 5C1, CA
PATENT APPLICANT(S): The University of Western Ontario, (University of Western Ontario, The; Western Ontario, The University

| | |
|---|---|
| | of; Ontario, The University of Western), Office of Industry Liason, Stevenson-Lawson Building, Room 319, London, Ontario N6A 5B8, CA |
| PATENT APPL. NUMBER: | 1820961 |
| AGENT: | Holliday, Louise Caroline, D Young & Co 120 Holborn, London EC1N 2DY, GB |
| AGENT NUMBER: | 95451 |
| LANGUAGE OF FILING: | English |
| LANGUAGE OF PUBL.: | English |
| LANGUAGE OF PROCEDURE: | English |
| LANGUAGE OF TITLE: | German; English; French |
| DOCUMENT TYPE: | Patent |
| PATENT INFO TYPE: | EPB1 Granted patent |
| PATENT INFORMATION: | |
| PATENT INFORMATION: | |

| NUMBER | KIND | DATE |
|---|---|---|
| NUMBER | KIND | DATE |
| EP 1131067 | B1 | 20040512 |
| WO 2000030635 | | 20000602 |

| | |
|---|---|
| DESIGNATED STATES: | AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE |
| APPLICATION INFO.: | EP 1999-955613 A 19991119 |
| | WO 1999-CA1106 A 19991119 |
| PRIORITY INFO.: | CA 1998-2254429 A 19981119 |

CITED NON PATENT LIT.:

KOYAMA E ET AL: "Retinoid signaling is required for chondrocyte maturation and endochondral bone formation during limb skeletogenesis." DEVELOPMENTAL BIOLOGY, (1999 APR 15) 208 (2) 375-91. , XP000879298;

PATENT ABSTRACTS OF JAPAN vol. 1998, no. 10, 31 August 1998 (1998-08-31) & JP 10 114757 A (SHUDO KOICHI), 6 May 1998 (1998-05-06);

STANDEVEN A M ET AL: "Retinoid-induced epiphyseal plate closure in guinea pigs." FUNDAMENTAL AND APPLIED TOXICOLOGY, (1996 NOV) 34 (1) 91-8. , XP000879170;

KOYAMA, E. ET AL: "Retinoids and their nuclear receptors promote the completion of chondrocyte maturation during limb skeletogenesis." MOLECULAR BIOLOGY OF THE CELL, (NOV., 1997) VOL. 8, NO. SUPPL., PP. 71A. MEETING INFO.: 37TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY WASHINGTON, D.C., USA DECEMBER 13-17, 1997 AMERICAN SOCIETY FOR CELL BIOLOGY. , XP000879148;

NUKA S (REPRINT) ET AL: "All-trans retinoic acid inhibits dexamethasone-induced ALP activity and mineralization in human osteoblastic cell line SV HFO" CELL STRUCTURE AND FUNCTION, (FEB 1997) VOL. 22, NO. 1, PP. 27-32. PUBLISHER: JAPAN SOC CELL BIOLOGY, SHIMOTACHIURI OGAWA-HIGASHI, KAMIKYOKU KYOTO 602, JAPAN. ISSN: 0386-7196., XP000879088 SAPPORO MED UNIV, SCH MED, DEPT PATHOL, CHUO KU, S1, W17, SAPPORO, HOKKAIDO 060, JAPAN (Reprint);SAPPORO MED UNIV, SCH MED, DEPT ORTHOPAED SURG, CHUO KU, SAPPORO, HOKKAIDO 060, JAPAN;

VON SCHROEDER H P ET AL: "The effects of natural and synthetic retinoids on the differentiation of RCJ C5.18 chondrogenic cells." TERATOLOGY, (1994 JUL) 50 (1) 54-62. , XP000653320;

JIANG: "Modulation of limb bud chondrogenesis by retinoic acid and retinoic acid receptors." DEVELOPMENTAL BIOLOGY, vol. 39, no. 4, 1995, XP000884176

| | |
|---|---|
| CITED PATENT LIT.: | WO 9808546 A |

WO 9924415 A
US 5827500 A

L2 ANSWER 11 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2000153508 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10684250
TITLE: Regulation of skeletal progenitor differentiation by the BMP and retinoid signaling pathways.
AUTHOR: Weston A D; Rosen V; Chandraratna R A; Underhill T M
CORPORATE SOURCE: Division of Oral Biology, School of Dentistry, The University of Western Ontario, London, Ontario, Canada.
SOURCE: Journal of cell biology, (2000 Feb 21) 148 (4) 679-90. Journal code: 0375356. ISSN: 0021-9525.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000327
Last Updated on STN: 20000327
Entered Medline: 20000313

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARalpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of BMPs, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or BMP-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that BMP and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a BMP-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L2 ANSWER 12 OF 18 MEDLINE on STN
ACCESSION NUMBER: 2000080294 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10614657
TITLE: Retinoic acid is a potent regulator of growth plate **chondrogenesis.**
AUTHOR: De Luca F; Uyeda J A; Mericq V; Mancilla E E; Yanovski J A; Barnes K M; Zile M H; Baron J
CORPORATE SOURCE: Developmental Endocrinology Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland 20892, USA.. fdeluca@peds.umaryland.edu
SOURCE: Endocrinology, (2000 Jan) 141 (1) 346-53. Journal code: 0375040. ISSN: 0013-7227.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 20000124
Last Updated on STN: 20000124
Entered Medline: 20000113

AB Vitamin A deficiency and excess both cause abnormalities in mammalian longitudinal bone growth. Because all-trans retinoic acid (RA) is synthesized from vitamin A, we hypothesized that RA regulates growth plate **chondrogenesis.** Consistent with this hypothesis, a single oral dose of RA reduced the height of the rat proximal tibial growth plate. To determine whether RA acts directly on growth plate, fetal rat metatarsal bones were cultured in the presence of RA. In this system, RA inhibited longitudinal bone growth by three mechanisms: 1) decreased chondrocyte proliferation, (assessed by 3H-thymidine incorporation), particularly in the proliferative zone of the growth plate; 2) decreased matrix synthesis (assessed by 35SO4 incorporation into glycosaminoglycans); and 3) decreased cell hypertrophy (determined histologically). The growth-inhibiting effects of RA were completely reversed by a retinoic acid receptor (**RAR**) **antagonist.** In the absence of exogenous RA, this antagonist accelerated bone growth, as did an RA-specific neutralizing antibody, suggesting that endogenous RA negatively regulates growth plate **chondrogenesis.** We conclude that RA, acting through RARs, negatively regulates longitudinal bone growth by inhibiting growth plate chondrocyte proliferation, chondrocyte hypertrophy, and matrix synthesis.

L2 ANSWER 13 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:142678 BIOSIS
DOCUMENT NUMBER: PREV200000142678
TITLE: Regulation of skeletal progenitor differentiation by the BMP and retinoid signaling pathways.
AUTHOR(S): Weston, Andrea D.; Rosen, Vicki; Chandraratna, Roshantha A. S.; Underhill, T. Michael [Reprint author]
CORPORATE SOURCE: School of Dentistry, Faculty of Medicine and Dentistry, University of Western Ontario, London, ON, N6A 5C1, Canada
SOURCE: Journal of Cell Biology, (Feb. 21, 2000) Vol. 148, No. 4, pp. 679-690. print.
CODEN: JCLBA3. ISSN: 0021-9525.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 19 Apr 2000
Last Updated on STN: 4 Jan 2002

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARalpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of BMPs, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or BMP-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that BMP and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a

BMP-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L2 ANSWER 14 OF 18 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:108847 BIOSIS
DOCUMENT NUMBER: PREV200000108847
TITLE: Retinoic acid is a potent regulator of growth plate **chondrogenesis.**
AUTHOR(S): De Luca, Francesco [Reprint author]; Uyeda, Jennifer A.; Mericq, Veronica; Mancilla, Edna E.; Yanovski, Jack A.; Barnes, Kevin M.; Zile, Maija H.; Baron, Jeffrey
CORPORATE SOURCE: Department of Pediatrics, University of Maryland School of Medicine, 22 South Greene Street, Room N5E13, Baltimore, MD, 21201-1595, USA
SOURCE: Endocrinology, (Jan., 2000) Vol. 141, No. 1, pp. 346-353. print.
CODEN: ENDOAO. ISSN: 0013-7227.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 22 Mar 2000
Last Updated on STN: 3 Jan 2002

AB Vitamin A deficiency and excess both cause abnormalities in mammalian longitudinal bone growth. Because all-trans retinoic acid (RA) is synthesized from vitamin A, we hypothesized that RA regulates growth plate **chondrogenesis.** Consistent with this hypothesis, a single oral dose of RA reduced the height of the rat proximal tibial growth plate. To determine whether RA acts directly on growth plate, fetal rat metatarsal bones were cultured in the presence of RA. In this system, RA inhibited longitudinal bone growth by three mechanisms: 1) decreased chondrocyte proliferation, (assessed by 3H-thymidine incorporation), particularly in the proliferative zone of the growth plate; 2) decreased matrix synthesis (assessed by 35SO4 incorporation into glycosaminoglycans); and 3) decreased cell hypertrophy (determined histologically). The growth-inhibiting effects of RA were completely reversed by a retinoic acid receptor (**RAR**) **antagonist.** In the absence of exogenous RA, this antagonist accelerated bone growth, as did an RA-specific neutralizing antibody, suggesting that endogenous RA negatively regulates growth plate **chondrogenesis.** We conclude that RA, acting through RARs, negatively regulates longitudinal bone growth by inhibiting growth plate chondrocyte proliferation, chondrocyte hypertrophy, and matrix synthesis.

L2 ANSWER 15 OF 18 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2001126677 EMBASE
TITLE: Retinoic acid is a potent regulator of growth plate **chondrogenesis.**
AUTHOR: De Luca F.; Uyeda J.A.; Mericq V.; Mancilla E.E.; Yanovski J.A.; Barnes K.M.; Zile M.H.; Baron J.
CORPORATE SOURCE: F. De Luca, Department of Pediatrics, Univ. of Maryland School of Medicine, 22 South Greene Street, Baltimore, MD 21201-1595, United States. fdeluca@peds.umaryland.edu
SOURCE: Endocrinology, (2000) Vol. 141, No. 1, pp. 346-353.
Refs: 42
ISSN: 0013-7227 CODEN: ENDOAO
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 003 Endocrinology
021 Developmental Biology and Teratology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20010419
Last Updated on STN: 20010419

AB Vitamin A deficiency and excess both cause abnormalities in mammalian longitudinal bone growth. Because all-trans retinoic acid (RA) is synthesized from vitamin A, we hypothesized that RA regulates growth plate **chondrogenesis.** Consistent with this hypothesis, a single oral dose of RA reduced the height of the rat proximal tibial growth plate. To determine whether RA acts directly on growth plate, fetal rat metatarsal bones were cultured in the presence of RA. In this system, RA inhibited longitudinal bone growth by three mechanisms: 1) decreased chondrocyte proliferation, (assessed by (3)H-thymidine incorporation), particularly in the proliferative zone of the growth plate; 2) decreased matrix synthesis (assessed by (35)SO(4) incorporation into glycosaminoglycans); and 3) decreased cell hypertrophy (determined histologically). The growth-inhibiting effects of RA were completely reversed by a retinoic acid receptor (**RAR**) **antagonist.** In the absence of exogenous RA, this antagonist accelerated bone growth, as did an RA-specific neutralizing antibody, suggesting that endogenous RA negatively regulates growth plate **chondrogenesis.** We conclude that RA, acting through RARs, negatively regulates longitudinal bone growth by inhibiting growth plate chondrocyte proliferation, chondrocyte hypertrophy, and matrix synthesis.

L2 ANSWER 16 OF 18 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000316638 EMBASE
TITLE: Regulation of skeletal progenitor differentiation by the BMP and retinoid signaling pathways.
AUTHOR: Weston A.D.; Rosen V.; Chandraratna R.A.S.; Underhill T.M.
CORPORATE SOURCE: T.M. Underhill, School of Dentistry, Faculty of Medicine/Dentistry, University of Western Ontario, London, Ont. N6A 5C1, Canada. tunderhi@julian.uwo.ca
SOURCE: Journal of Cell Biology, (21 Feb 2000) Vol. 148, No. 4, pp. 679-690.
Refs: 63
ISSN: 0021-9525 CODEN: JCLBA3
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 021 Developmental Biology and Teratology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 20000921
Last Updated on STN: 20000921

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RARα in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E., C.B. Bock, K. Schughart, E. Linney, and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of BMPs, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or BMP-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that BMP and RAR-signaling pathways appear to operate independently to coordinate

skeletal development, and that retinoid signaling can function in a BMP-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L2 ANSWER 17 OF 18 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:170484 SCISEARCH
THE GENUINE ARTICLE: 287NB
TITLE: Regulation of skeletal progenitor differentiation by the BMP and retinoid signaling pathways
AUTHOR: Weston A D; Rosen V; Chandraratna R A S; Underhill T M (Reprint)
CORPORATE SOURCE: Univ Western Ontario, Sch Dent, Fac Med & Dent, Div Oral Biol, London, ON N6A 5C1, Canada (Reprint); Univ Western Ontario, Dept Physiol, Fac Med & Dent, London, ON N6A 5C1, Canada; Genet Inst Inc, Cambridge, MA 02140 USA; Allergan Pharmaceut Inc, Retinoid Res Grp, Irvine, CA 92623 USA
COUNTRY OF AUTHOR: Canada; USA
SOURCE: JOURNAL OF CELL BIOLOGY, (21 FEB 2000) Vol. 148, No. 4, pp. 679-690.
ISSN: 0021-9525.
PUBLISHER: ROCKEFELLER UNIV PRESS, 1114 FIRST AVE, 4TH FL, NEW YORK, NY 10021 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 63
ENTRY DATE: Entered STN: 2000
Last Updated on STN: 2000

*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB The generation of the paraxial skeleton requires that commitment and differentiation of skeletal progenitors is precisely coordinated during limb outgrowth. Several signaling molecules have been identified that are important in specifying the pattern of these skeletal primordia. Very little is known, however, about the mechanisms regulating the differentiation of limb mesenchyme into chondrocytes. Overexpression of RAR alpha in transgenic animals interferes with **chondrogenesis** and leads to appendicular skeletal defects (Cash, D.E,, C.B, Beck, K. Schughart, E, Linney: and T.M. Underhill. 1997. J. Cell Biol. 136:445-457). Further analysis of these animals shows that expression of the transgene in chondroprogenitors maintains a prechondrogenic phenotype and prevents chondroblast differentiation even in the presence of BMPs, which are known stimulators of cartilage formation. Moreover, an **RAR antagonist** accelerates chondroblast differentiation as demonstrated by the emergence of collagen type II-expressing cells much earlier than in control or BMP-treated cultures. Addition of Noggin to limb mesenchyme cultures inhibits cartilage formation and the appearance of precartilaginous condensations. In contrast, abrogation of retinoid signaling is sufficient to induce the expression of the chondroblastic phenotype in the presence of Noggin. These findings show that BMP and RAR-signaling pathways appear to operate independently to coordinate skeletal development, and that retinoid signaling can function in a BMP-independent manner to induce cartilage formation. Thus, retinoid signaling appears to play a novel and unexpected role in skeletogenesis by regulating the emergence of chondroblasts from skeletal progenitors.

L2 ANSWER 18 OF 18 SCISEARCH COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:3683 SCISEARCH
THE GENUINE ARTICLE: 267AJ
TITLE: Retinoic acid is a potent regulator of growth plate **chondrogenesis**
AUTHOR: De Luca F (Reprint); Uyeda J A; Mericq V; Mancilla E E; Yanovski J A; Barnes K M; Zile M H; Baron J

CORPORATE SOURCE: Univ Maryland, Sch Med, Dept Pediat, 22 S Greene St, Room N5E13, Baltimore, MD 21201 USA (Reprint); NICHHD, Dev Endocrinol Branch, NIH, Bethesda, MD 20892 USA; Michigan State Univ, Dept Food Sci & Human Nutr, E Lansing, MI 48824 USA
COUNTRY OF AUTHOR: USA
SOURCE: ENDOCRINOLOGY, (JAN 2000) Vol. 141, No. 1, pp. 346-353. ISSN: 0013-7227.
PUBLISHER: ENDOCRINE SOC, 4350 EAST WEST HIGHWAY SUITE 500, BETHESDA, MD 20814-4110 USA.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 42
ENTRY DATE: Entered STN: 2000
Last Updated on STN: 2000
*ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Vitamin A deficiency and excess both cause abnormalities in mammalian longitudinal bone growth. Because all-trans retinoic acid (RA) is synthesized from vitamin A, we hypothesized that RA regulates growth plate **chondrogenesis.** Consistent with this hypothesis, a single oral dose of RA reduced the height of the rat proximal tibial growth plate. To determine whether RA acts directly on growth plate, fetal rat metatarsal bones were cultured in the presence of RA. In this system, RA inhibited longitudinal bone growth by three mechanisms: 1) decreased chondrocyte proliferation, (assessed by H-3-thymidine incorporation), particularly in the proliferative zone of the growth plate; 2) decreased matrix synthesis (assessed by (SO4)-S-35 incorporation into glycosaminoglycans); and 3) decreased cell hypertrophy (determined histologically). The growth-inhibiting effects of RA were completely reversed by a retinoic acid receptor (**RAR**) **antagonist.** In the absence of exogenous RA, this antagonist accelerated bone growth, as did an RA-specific neutralizing antibody, suggesting that endogenous RA negatively regulates growth plate **chondrogenesis.** We conclude that RA, acting through RARs, negatively regulates longitudinal bone growth by inhibiting growth plate chondrocyte proliferation, chondrocyte hypertrophy, and matrix synthesis.

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(FILE 'HOME' ENTERED AT 13:04:38 ON 31 AUG 2005)

FILE 'CAPLUS, USPATFULL, JAPIO, EPFULL, MEDLINE, BIOSIS, EMBASE, SCISEARCH' ENTERED AT 13:15:27 ON 31 AUG 2005
L1 527 S (RAR ANTAGONIST#)
L2 18 S L1 AND CHONDROGEN?

=> s l2 and (AGN 194301)
L3 4 L2 AND (AGN 194301)

=> d l3 1-4 ibib abs

L3 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:368088 CAPLUS
DOCUMENT NUMBER: 133:828
TITLE: Composition and use of **RAR antagonists** for promoting **chondrogenesis**
INVENTOR(S): Underhill, Tully Michael; Weston, Andrea Dawn
PATENT ASSIGNEE(S): The University of Western Ontario, Can.
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|---|---|---|
| WO 2000030635 | A1 | 20000602 | WO 1999-CA1106 | 19991119 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2349555 | AA | 20000602 | CA 1999-2349555 | 19991119 |
| EP 1131067 | A1 | 20010912 | EP 1999-955613 | 19991119 |
| EP 1131067 | B1 | 20040512 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| JP 2002530331 | T2 | 20020917 | JP 2000-583518 | 19991119 |
| AU 764394 | B2 | 20030814 | AU 2000-12552 | 19991119 |
| AU 2000012552 | A5 | 20000613 | | |
| AT 266396 | E | 20040515 | AT 1999-955613 | 19991119 |
| ES 2219076 | T3 | 20041116 | ES 1999-955613 | 19991119 |
| CA 2357549 | AA | 20020321 | CA 2001-2357549 | 20010921 |
| US 2002061514 | A1 | 20020523 | US 2001-957456 | 20010921 |
| HK 1041633 | A1 | 20041008 | HK 2002-101649 | 20020304 |
| PRIORITY APPLN. INFO.: | | | CA 1998-2254429 A | 19981119 |
| | | | WO 1999-CA1106 W | 19991119 |
| | | | US 2000-234242P P | 20000921 |

AB The invention provides compns. comprising a **RAR antagonist** for promoting **chondrogenesis**, as well as methods employing such compns. for treating cartilage and associated bone abnormalities resulting from injury or disease and for ex vivo tissue engineering.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 4 USPATFULL on STN
ACCESSION NUMBER: 2005:11733 USPATFULL
TITLE: Retinoid receptor pan-antagonists for stimulating **chondrogenesis**
INVENTOR(S): Underhill, Michael Tully, Ontario, CANADA
Weston, Andrea D, Ontario, CANADA

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 2005009868 | A1 | 20050113 | |
| APPLICATION INFO.: | US 2004-489750 | A1 | 20040827 | (10) |
| | WO 2002-CA1421 | | 20020917 | |

| | NUMBER | DATE |
|---|---|---|
| PRIORITY INFORMATION: | US 2001-322874P | 20010917 (60) |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 20
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 10 Drawing Page(s)
LINE COUNT: 1777
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The invention relates to methods and compositions for inducing or enhancing **chondrogenesis** in vivo and/or ex vivo. More specifically, the invention is directed to the use of RAR pan-antagonist compositions for the treatment, repair and engineering of cartilage.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 3 OF 4 USPATFULL on STN
ACCESSION NUMBER: 2003:181419 USPATFULL
TITLE: Compositions and methods for affecting osteogenesis
INVENTOR(S): Underhill, T. Michael, Ontario, CANADA
Sampaio, Arthur V., Ontario, CANADA
Weston, Andrea D., Ontario, CANADA

| | NUMBER | KIND | DATE | |
|---|---|---|---|---|
| PATENT INFORMATION: | US 2003125252 | A1 | 20030703 | |
| APPLICATION INFO.: | US 2002-221602 | A1 | 20020912 | (10) |
| | WO 2001-CA317 | | 20010313 | |

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MYERS BIGEL SIBLEY & SAJOVEC, PO BOX 37428, RALEIGH, NC, 27627
NUMBER OF CLAIMS: 72
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 1833
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention relates to compositions for promoting and inhibiting osteogenesis and to methods for treating bone abnormalities resulting from injury, toxicity or disease and for ex vivo bone tissue engineering.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L3 ANSWER 4 OF 4 EPFULL COPYRIGHT 2005 EPO/FIZ KA on STN

ACCESSION NUMBER: 1999:96730 EPFULL
UPDATE DATE PUBLICAT.: 20050504
DATA UPDATE DATE: 20050504
DATA UPDATE WEEK: 200518
TITLE (ENGLISH): COMPOSITION AND USE OF **RAR ANTAGONISTS** FOR PROMOTING **CHONDROGENESIS**
TITLE (FRENCH): COMPOSITION A BASE D'ANTAGONISTES DES RAR ET SON UTILISATION POUR FAVORISER LA **CHONDROGENESE**
TITLE (GERMAN): ZUBEREITUNG UND VERWENDUNG VON RAR ANTAGONISTEN ZUR FORDERUNG DER **CHONDROGENESE**
INVENTOR(S): UNDERHILL, Tully Michael, Univ. Western of Ontario, Div. of Oral Biology, School of Dentistry, London, Ontario N6A 5C1, CA; WESTON, Andrea, Dawn, Univ.of Western Ontario, The Faculty of Med. & Dentistry, Dep.of Phys., London, Ontario N6A 5C1, CA
PATENT APPLICANT(S): The University of Western Ontario, (University of Western Ontario, The; Western Ontario, The University of; Ontario, The University of Western), Office of Industry Liason, Stevenson-Lawson Building, Room 319, London, Ontario N6A 5B8, CA
PATENT APPL. NUMBER: 1820961
AGENT: Holliday, Louise Caroline, D Young & Co 120 Holborn, London EC1N 2DY, GB
AGENT NUMBER: 95451
LANGUAGE OF FILING: English
LANGUAGE OF PUBL.: English

LANGUAGE OF PROCEDURE: English
LANGUAGE OF TITLE: German; English; French
DOCUMENT TYPE: Patent
PATENT INFO TYPE: EPB1 Granted patent
PATENT INFORMATION:
PATENT INFORMATION:

| NUMBER | KIND | DATE |
|---|---|---|
| NUMBER | KIND | DATE |
| EP 1131067 | B1 | 20040512 |
| WO 2000030635 | | 20000602 |

DESIGNATED STATES: AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU MC NL PT SE

APPLICATION INFO.:
EP 1999-955613 A 19991119
WO 1999-CA1106 A 19991119

PRIORITY INFO.: CA 1998-2254429 A 19981119

CITED NON PATENT LIT.:

KOYAMA E ET AL: "Retinoid signaling is required for chondrocyte maturation and endochondral bone formation during limb skeletogenesis." DEVELOPMENTAL BIOLOGY, (1999 APR 15) 208 (2) 375-91. , XP000879298;

PATENT ABSTRACTS OF JAPAN vol. 1998, no. 10, 31 August 1998 (1998-08-31) & JP 10 114757 A (SHUDO KOICHI), 6 May 1998 (1998-05-06);

STANDEVEN A M ET AL: "Retinoid-induced epiphyseal plate closure in guinea pigs." FUNDAMENTAL AND APPLIED TOXICOLOGY, (1996 NOV) 34 (1) 91-8. , XP000879170;

KOYAMA, E. ET AL: "Retinoids and their nuclear receptors promote the completion of chondrocyte maturation during limb skeletogenesis." MOLECULAR BIOLOGY OF THE CELL, (NOV., 1997) VOL. 8, NO. SUPPL., PP. 71A. MEETING INFO.: 37TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR CELL BIOLOGY WASHINGTON, D.C., USA DECEMBER 13-17, 1997 AMERICAN SOCIETY FOR CELL BIOLOGY. , XP000879148;

NUKA S (REPRINT) ET AL: "All-trans retinoic acid inhibits dexamethasone-induced ALP activity and mineralization in human osteoblastic cell line SV HFO" CELL STRUCTURE AND FUNCTION, (FEB 1997) VOL. 22, NO. 1, PP. 27-32. PUBLISHER: JAPAN SOC CELL BIOLOGY, SHIMOTACHIURI OGAWA-HIGASHI, KAMIKYOKU KYOTO 602, JAPAN. ISSN: 0386-7196., XP000879088 SAPPORO MED UNIV, SCH MED, DEPT PATHOL, CHUO KU, S1, W17, SAPPORO, HOKKAIDO 060, JAPAN (Reprint);SAPPORO MED UNIV, SCH MED, DEPT ORTHOPAED SURG, CHUO KU, SAPPORO, HOKKAIDO 060, JAPAN;

VON SCHROEDER H P ET AL: "The effects of natural and synthetic retinoids on the differentiation of RCJ C5.18 chondrogenic cells." TERATOLOGY, (1994 JUL) 50 (1) 54-62. , XP000653320;

JIANG: "Modulation of limb bud chondrogenesis by retinoic acid and retinoic acid receptors." DEVELOPMENTAL BIOLOGY, vol. 39, no. 4, 1995, XP000884176

CITED PATENT LIT.:
WO 9808546 A
WO 9924415 A
US 5827500 A

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